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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,510	10/31/2003	Patricia Grasso	19705-001CIP	9600

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,510	GRASSO ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *17-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/31/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-16 and 28-31 (product) in the reply filed on 05/03/2006, is acknowledged. Claims 17-27 are withdrawn as being drawn to non-elected subject matter. Claims 1-16 and 28-31 are examined on the merits.

Priority

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 09/377,081 (now US 6,777,388) and provisional thereof, 60/097,457, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Although '081 and '457 discuss the motivation for D-amino acid substitutions in peptides generally (by literature review) and rationale for their substitution in leptins generally (see para 36, lines 21-52 of US 6,777,388), the descriptions do not expressly describe the same as applied to the fragments SEQ ID NOS: 2 or 18 or specific residues therein, such as D-Leu-4 and D-Pro-5 (see e.g. claims 1, 10-11, 15-16, and 28 respectively).

However, disclosure of the invention sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*,

38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994) was found in provisional application 60/422,723, filed 10/31/2002; the earliest effective filing date to which priority was deemed present as applied to the presently claimed subject matter.

Specification

The disclosure is objected to because of the following informalities: on specification page 52, line 14 and page 82, line 1, the phrase --(SEQ ID NO: 2)-- is required to be inserted after said peptide sequence.

Appropriate correction by amendment is required.

Applicant's cooperation is requested in correcting any other SEQ ID NO: omissions or minor errors, which applicant may become aware in the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-12, 14, and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/46585 (SmithKline Beecham, P.L.C.) alone; or in view of any of Doherty et al. (1993, J. Med. Chem., 36: 2585-2594); Kirby et al. (1993, J. Med. Chem. 36: 3802-3808); Morita et al. (1994, FEBS Lett. 353: 84-88); Wang et al. (1993, Int. J.Pept. Protein Res. 42: 392-399); Fauchere and Thiunieau (1992, Adv. Drug Res. 23: 127-159); or Leng et al. (1996, Pept.

Res. 9: 189-194); and further in view of DeGrado (1988, Adv. Protein Chem., 39:51-124); or Rose et al. (1985, Adv. Protein Chem., 37:1-109) [all eight secondary references described in relevant literature review of peptide chemistry in col. 36 of '388].

WO 97/46585 teach peptides comprising native leptin (LEP or OB protein) fragments, such as residues 116-149 of OB (e.g. which includes Applicant's OB3 or OB-3, SEQ ID NO: 18); and functional derivatives, analogues, and variants thereof (e.g. which would include related comparison species such as murine/mouse SEQ ID NO: 2); including peptides where one or more amino acids of the peptides mentioned herein are replaced with alternative amino acids, wherein said alternative amino acids includes *amino acids of alternative stereochemistry* to the amino acids in ob protein (e.g. D-isoform); and *cyclized* (See page 2.

[NOTE 1: stereochemistry = [t]he arrangement of atoms in a molecule in three-dimensional space, especially with regard to the differences between enantiomers. The arrangements are specified in chemical formulas with the letters R, S, L, and/or D. [ ] L and D designations are given if the enantiomers have optical activity, that is, if they will rotate polarized light. The member of the pair which rotates polarized light clockwise is dextrorotatory, or D, and the member of the pair which rotates polarized light counterclockwise is levorotatory, or L (there is always one of each in every pair). This is also often referred to as handedness, where D is right-handed and L is lefthanded. See Online Medical Dictionary, 11/13/1997, http://cancerweb.ncl.ac.uk/cgi-bin/omd?stereochemical+ configuration; cited merely to indicate stereochemistry refers to L versus D isoforms].

[NOTE 2: WO 97/46585, although contemplating fragments of residues 116-149 of OB; does not teach or contain motivation for a peptide *consisting of* SEQ ID NOS: 2 or 18, e.g. Applicant's claims 2, 13, 15-16].

Doherty et al., Kirby et al., Morita et al., Wang et al., Fauchere and Thiunieau, and Leng et al. all teach the substitution of native L-isoform peptides with D-isoform amino acids at any one or more residues of the same peptide sequence, in order to increase the resistance of peptides to enzymatic hydrolysis and/or enhance one or more properties of biologically active peptides such as receptor binding, functional potency, duration of action, or stability (e.g. as shown in the synthetic glycoprotein hormone antagonist of Leng et al.).

DeGrado and Rose et al. teach that cyclization of native peptides is used to increase potency, selectivity, and stability of any peptide (e.g. including D-isoform peptides).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute a peptide comprising native L-isoform SEQ ID NOS: 2 or 18 with one or more D-isoform amino acids and cyclize the same, in WO 97/46585 alone, because WO 97/46585 advantageously teach that the OB may be in D-isoform and cyclized. Alternatively, any of Doherty et al., Kirby et al., Morita et al., Wang et al., Fauchere and Thiunieau, or Leng et al. advantageously provide motivation for one of ordinary skill in the art to take a known native L-isoform peptide and substitute a D-isoform amino acid at any one or more residues of the same peptide sequence, in order to increase the resistance of peptides to enzymatic hydrolysis and/or enhance one or more properties of biologically active peptides such as receptor binding, functional potency, duration of action, or stability (e.g. as shown in the synthetic glycoprotein hormone antagonist of Leng et al.). Additionally, either DeGrado or Rose et al. advantageously

provide motivation for one of ordinary skill in the art to cyclize any peptide (which would include D-isoform peptides) in order to likewise increase potency, selectivity, and stability thereof. The motivational nexus between these references and X is the contemplation of X for improved analogs and the accepted desire of skilled artisans to make native peptides ever more biologically compatible/effective, through known means such D-isomerization and cyclization. [It is noted that the elected invention claims are to a product, and that the additional claim language in these claims to inherent/intrinsic properties and/or intended use of said product, do not impute patentable limitations/consideration into said product. As to the intended use language, nothing would preclude the use of products in the art, cited above, for such use].

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16 and 28-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,777,388 in view of WO 97/46585 (SmithKline Beecham, P.L.C.), or any of Doherty et al. (1993, J. Med. Chem., 36: 2585-2594); Kirby et al. (1993, J. Med. Chem. 36: 3802-3808); Morita et al. (1994, FEBS Lett. 353: 84-88); Wang et al. (1993, Int. J.Pept. Protein Res. 42: 392-399); Fauchere and Thiunieau (1992, Adv. Drug Res. 23: 127-159); or Leng et al. (1996, Pept. Res. 9: 189-194); and further in view of DeGrado (1988, Adv. Protein Chem., 39:51-124); or Rose et al. (1985, Adv. Protein Chem., 37:1-109) [all eight secondary references described in relevant literature review of peptide chemistry in col. 36 of '388]. All the references are discussed above under 35 USC section 103.

Claims 1-6 of '388 describe peptides consisting of SEQ ID NOS: 2 or 18 (species of Applicant's currently claimed genus of peptides "comprising" the same SEQ ID NOS: 2 or 18), while WO 97/46585 advantageously provide motivation for peptides comprising OB functional derivatives comprising D-isoforms and the cyclization thereof. Alternatively any of Doherty et al., Kirby et al., Morita et al., Wang et al., Fauchere and Thiunieau, or Leng et al. advantageously provide motivation for one of ordinary skill in the art to take a known native L-isoform peptide and substitute a D-isoform amino acid at any one or more residues of the same peptide sequence, in order to increase the resistance of peptides to enzymatic hydrolysis and/or enhance one or

more properties of biologically active peptides such as receptor binding, functional potency, duration of action, or stability (e.g. as shown in the synthetic glycoprotein hormone antagonist of Leng et al.). Additionally, either DeGrado or Rose et al. advantageously provide motivation for one of ordinary skill in the art to cyclize any peptide (which would include D-isoform peptides) in order to likewise increase potency, selectivity, and stability thereof. The motivational nexus between these references and '388 is the desire of skilled artisans to make native peptides ever more biologically compatible/effective, through known means such D-isomerization and cyclization.

Claim Rejections - 35 USC § 112 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 15-16, and 28-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to OB3 (or OB-3) lexicography identified compounds. However, specification page 8 is drawn to OB-3 (assumed to be the same as OB3), which identifies either mouse (SEQ ID NO: 2) or human (SEQ ID NO: 18) leptin, which are each distinct peptides sequences. Thus, when claiming the compound by OB3, it is unclear whether mouse SEQ ID NO: 2 or human SEQ ID NO: 18 is being claimed? Furthermore, the claims are drawn confusingly to "OB3", while the specification is drawn to "OB-3". Although the latter does not necessarily rise to the level of being indefinite, Applicant should maintain consistency throughout the specification and claims, as either OB3 or OB-3.

Claims 28-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Namely, although the elected invention claims are to a product, and claim language to inherent/intrinsic properties and/or intended use of said product, do not impute patentable limitations into said product; it is nevertheless unclear how the administration of the same product can equally reduce serum insulin levels as well as blood glucose levels (two blood or serum counterbalancing compounds). In order to address this indefinite language, Applicant is asked to amend the above discrepancy or explain in the response how the aforementioned is possible (though neither form of addressing this claim language discrepancy will bear substantive weight as to the patentability of the product, as noted above).

Observation

Applicant may wish to consider amending claims 1-16 and 28-31, commensurate in scope with the '388 patent (e.g. consisting of SEQ ID NOS: 2 or 18), but drawn to the D-isoforms thereof; in combination with the filing of a Terminal Disclaimer over the '388 patent.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 08/19/2009

MAURY AUDET
PATENT EXAMINER
ART UNIT 1654